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| 10/582,794 | 10/31/2006 | Jens Christian Norrild | 141-451 | 7176 |

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NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

| EXAMINER | |
|---|---|
| HANLEY, SUSAN MARIE | |
| ART UNIT | PAPER NUMBER |
| 1651 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/582,794 | NORRILD ET AL. | |
| | Examiner | Art Unit | |
| | SUSAN HANLEY | 1651 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *33-64* is/are pending in the application.

4a) Of the above claim(s) *55-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/27/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 33-64 are pending.

### *Election/Restrictions*

Group I, claims 33-54, $R^1$ and $R^2$ $NMe_2$; $R^3$ = attached to a linker structure, $N(Me)(CH_2)_3(C=O)$-link to aminodextran,;$R^4$-$R^9$=H; $R^{10}$-$R^{15}$=OMe; the energy acceptor and energy donor are linked together by non-covalent bonding; the analyte analog is amino dextran; a linker is present. The linker is $N(Me)(CH_2)_3(C=O)$-; the linker is formed by the reaction of the succinimidyl active ester in HMCV-1 in the reply filed on 7/13/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The specie election is withdrawn and the genus of group I is examined.

Claims 55-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

### *Specification*

The use of the trademarks CSY 21® and Alexa Fluor 594® have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Independent claim 33 is drawn to a reagent for use in detecting an analyte comprising a fluorescent energy donor and an energy acceptor wherein the energy acceptor has the general formula shown in claim 33. The energy donor and acceptor are linked covalently or non-covalently. Non-covalent bonding is disreputable by a suitable analyte that can be a glucose analog that can be dextran. The covalent bonding is cleavable. The energy acceptor and donor can be linked via a polynucleotide analog or polypeptide sequence wherein the sequence has a conformation that is capable of modulation by a suitable analyte as to modulate the distance between the energy donor and acceptor. Electron donating and electron withdrawing substituents are recited. One or more of the R groups can form bridging groups between rings. The reagent further comprises a counterion. The linker structure is formed by linker element and a reaction partner that are defined in claims 51-54. The energy donor is Alexa Fluor 594®.

The extremely broad genus structure of said claims does not have sufficient description in the specification, nor are a representative number of compounds described to demonstrate that applicant was in possession of the genus at the time of filing.

The claims are also drawn to analogs of analytes such as glucose and dextran as well as polynucleotide linkers. The extremely broad genus term “analogs” does not have sufficient description in the specification, nor are a representative number of compounds described within the genus to demonstrate that applicant was in possession at the time of filing the genus term “analog”.

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents" of the University of California v. Eli Lilly & Co.* the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or]

chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers,* 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe,* 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents" of the University of California v. Eli Lilly & Co.,* 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitutes a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli,* the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli,* 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation

between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for *a prima facie* case are discussed below.

**(1) Level of skill and knowledge in the art:**

The level of skill and knowledge in the art is high.

**(2) Partial structure:**

The specification discloses only the structures HMCV-1, HMCV-2 and HMCV-3 (specification pages 19, 21 and 26, respectively). The specification teaches that HMCV-1 was linked to amino dextran as the glucose analog and that Alexa Fluor 594® was attached to Concanavalin A (Con A) as the sugar binding lectin. The non-covalent binding between the donor and acceptor is disrupted by the bonding of the glucose analyte to the Concanavalin A, thus causing FRET (page 9 of the specification). The HCVM acceptor moiety is linked non-covalently to the acceptor. The specification discloses no other partial structures of compounds belonging to the extremely broad genus of compounds encompassed by the structure compound 33 and its dependent claims. There is no disclosure related to acceptor and donors that are covalently coupled. There is no disclosure related to any molecules wherein the phenyl rings are linked by bridging groups.

"Analog" is not defined in the specification so it is not clear how it is related to glucose, dextran or polynucleotide linkers or what is meant by "analog".

**(3) Physical and/or chemical properties and (4) Functional characteristics:**

The physical and chemical properties and functional characterisitc are only set forth for the HCVM species linked to amino dextran wherein the donor is Alexa Fluor 594® linked to Con A. The assay method is described only for HCVM species linked to amino dextran wherein the donor is Alexa Fluor 594® linked to Con A. The assay method describes the FRET assay wherein the binding of glucose to the Alexa Fluor 594®-lectin disrupts the non-covalent binding of the donor/acceptor specie. Applicant has not set forth the physical and/or chemical properties and functional for any other possible compounds embraced by the broad genus structure of the indicated claims.

With the exception of the HCVM-amino dextran molecule, Applicant has not set forth the physical and/or chemical properties and functional characteristics for other analogs of glucose or dextran.

the specification does not describe any partial structures of polynucleotide analogs.

**(5) Method of making the claimed invention:**

The specification describes only how to make the HCVM-1, HCVM-2 and HCVM-3 wherein the HCVM nucleus is linked to amino dextrans and the donor Alexa Fluor 594® is linked to Con A. There is no disclosure regarding the making of any other possible compound embraced by the indicated claims.

There is no disclosure related to the making of other analogs of glucose or dextran.

There is no disclosure related to the making of analogs of polynucleotides.

As stated *supra,* the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that **the indicated claims** are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless. Although the claims may recite some chemical/physical/functional characteristics of the genus, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of HCVM-1, HCVM-2 and HCVM-3 linked to amino dextran as the glucose analog and energy acceptor and Alexa Fluor 594 linked to Con A as the energy donor, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the structure of the indicated claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder,* 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide

adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claims 33-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for HCVM-1, HCVM-2 and HCVM-3 linked to amino dextran as the glucose analog and energy acceptor and Alexa Fluor 594® linked to Concanavalin A as the energy donor, does not reasonably provide enablement for the compounds embraced by the structure of claim 33 and said dependent claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright,* 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

[1]As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is “undue”, not “experimentation”.

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands',* 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Exparte Forman,* 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of those in the art,
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108,427 F.2d 833,839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands" factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art

The invention relates to a reagent for use in detecting an analyte comprising a fluorescent energy donor and an energy acceptor wherein the energy acceptor has the structure of the formula in claim 33. The energy donor and acceptor are linked covalently or non-covalently. Non-covalent bonding is disreputable by a suitable analyte that can be a glucose analog that can be dextran. The covalent bonding is cleavable. The energy

acceptor and donor are linked via a polynucleotide analog or polypeptide sequence wherein the sequence has a conformation that is capable of modulation by a suitable analyte as to modulate the distance between the energy donor and acceptor. Electron donating and electron withdrawing substituents are recited. One or more of the R groups can formed bridging groups between rings. The reagent further comprises a counterion. The linker structure is formed by linker element and a reaction partner that are defined in claims 51-54. The energy donor is Alexa Fluor 594®.

The relative skill of those in the art is high, generally that of a PhD organic chemist.

That factor is outweighed however by the unpredictalbe nature of the art. Synthetic organic chemistry involves the reaction of chemical entities to make desired products. However, the art is unpredictalbe due to unknown factors that can influence a chemical reaction. That is, one must consider the chemical and physical properties of the reactants and products, the reaction conditions and the desired course of the reaction. Any of these factors can have unknown or hidden aspects that will confound the predicted course of a reaction. There is no way for one skill in the art to know, a priori, if a given an unknown chemical reaction will proceed to the desired reaction products with a reasonable expectation of results. Thus, the state of the prior art does not support the broad scope of the above claims.

2. The breadth of the claims

The claims are broad insofar as they disclose a reagent for use in detecting an analyst comprising a fluorescent energy donor and an energy acceptor wherein the energy acceptor has the formula shown in claim 33.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification discloses only how to make and use HCVM species linked to amino dextran and Alexa Fluor 594® linked to Con A. The specification fails to teach how to make any other compound that belongs to the extremely broad genus belong to the structure of the indicated claims. the structure of claim 33 has multiple reactive sites and the neither disclosure nor the prior art teach how to control the reaction to direct the reaction to desired vs. undesired sites.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed supra) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that one of skill in the art could be predictably synthesize the compounds belonging the genus of the indicated claims as inferred in the claims and contemplated by the specification.

Genentech Inc. vs. Nova Nordisk states, "[A] patent is not a hunting license. It is not a reward for a search but a compensation for its successful conclusion and 'patent protection' is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" (42 USPQ 2d 1001, Fed. Circuit 1997).

To practice the invention of the instant claims required undue experimentation due to unpredictability in the synthesis of organic compounds and the lack of direction from Applicants regarding procedures for the formation of the full scope of the compounds of the claimed genus, preparing such would require undue experimentation. The amount of experimentation required in order to produce the compounds of the claimed genus is extremely large and the methodology of the production of the claimed compounds would required inventive effort and extensive experimental burden.

In light of the above discussion, the instant claims do not comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-54 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected because the metes and bounds of the term "general" are unclear. “General” implies that there are other modification that are not defined by the claims per se. That is, it is confusing as to what those additions or deletions might be.

Claim 54 contains the trademark/trade name Alexa Fluor 594®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe Alexa Fluor 594® and, accordingly, the identification/description is indefinite.

Claims 2-53 are rejected because they are dependent claims that do not overcome the deficiencies of the rejected independent claim from which they depend.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN HANLEY whose telephone number is (571)272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sandra Saucier/
Primary Examiner, Art Unit 1651

/Susan Hanley/
Examiner, Art Unit 1651